Evidence-based medicine: old French wine with a new Canadian label?

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In the past decade, 'evidence-based medicine' has come to represent a systematic approach to published research as the basis of clinical decisions. Coined at McMaster University Medical School in Canada, the term has spread globally[1–8]. It is used widely in discussion of clinical practice, and entire journals are devoted to the doctrines espoused. The movement has had opponents too. In this paper I discuss a similar movement that spread in the opposite direction—from the Old World to the New—in the early decades of the last century. The arguments that raged then seem all too familiar.

THE 'ONLY TRUE METHOD OF INVESTIGATION'

Introducing an article[5] in the *American Journal of Medical Sciences*, 1836, the editor, Elisha Bartlett, did not hesitate to pronounce it 'one of the most important medical works of the present century' marking the start of a new era in science. It was 'the first formal exposition of the results of the *only true method of investigation* [emphasis mine] in regard to the therapeutic value of remedial agents' and thus 'after centuries of an existence partaking somewhat of the mixed character of a sickly and rickety infancy, and an ignorant and half crazed manhood', medical science was maturing and could legitimately take its place amongst other sciences that had been more advanced.

The article that evoked such effusive praise was entitled 'Researches on the effects of blood-letting in some Inflammatory Diseases and on the influence of tartarised antimony and vesication in pneumonitis.' It was an adaptation of a book written by P Ch A Louis, translated into English by C G Putnam with a preface and appendix by James Jackson, MD, a physician at the Massachusetts General Hospital[6]. The report itself was a summary of some of the key findings with added comments by the editor himself.

LOUIS: THE DEVELOPMENT OF THE NUMERICAL METHOD

The author, Pierre Charles Alexandre Louis was born at Ai (now Ay) on the Marne on 11 April 1787. The son of a vineyard owner, Louis was sent to study law, but did not find it appealing and so turned to medicine, first at Rheims and later at Paris, graduating in 1817. With that degree he wandered around Russia for three years before settling in Odessa for a further four years. During that time he received the title of Physician to the Czar. When he had to deal with an epidemic of diphtheria, Louis realized how inadequate his knowledge was. So he decided to return to Paris where he began to study under an influential physician, Broussais[7–11].

The stint convinced Louis that even celebrated physicians did not know much and the didactic approach adopted by his mentor did not appeal to him. He decided to learn on his own from the patients themselves. One of Louis' classmates, Chomel, permitted him to work in two of the wards at La Charité Hospital. So, at the ripe age of 34, Louis set to work as a clinical clerk without pay for seven years. He is said to have worked up to five hours a day, devoting two hours to each necropsy and collecting over 2000 observations. Obsessed with the gathering of facts, Louis developed a systematic approach to collecting information. He did not select cases but took them as they were presented since he did not want to gather support for any doctrine. His guiding motto was 'Ars medica tota in observationibus'[11].

Louis scrupulously charted the course of a disease, looking as carefully as he could at the precise onset, listing all possible contributory factors, examining the patient thoroughly, noting signs and symptoms and monitoring the effects of all treatments. If the patient died a careful necropsy was done and the findings were recorded. Essentially he set out to build a comprehensive picture of the natural history of a disease based on observations from many cases, refusing to distil general principles till the facts had been gathered. This was the quintessential Baconian approach. The vast amount of data gathered permitted him to make comparisons and systematically evaluate the efficacy of treatments. Louis stated categorically that 'a therapeutic agent cannot be employed with any discrimination or probability of success in a given case, unless its general efficacy, in analogous cases, has been previously ascertained', and thus, 'without the aid of statistics nothing like real medicine is possible'[12].

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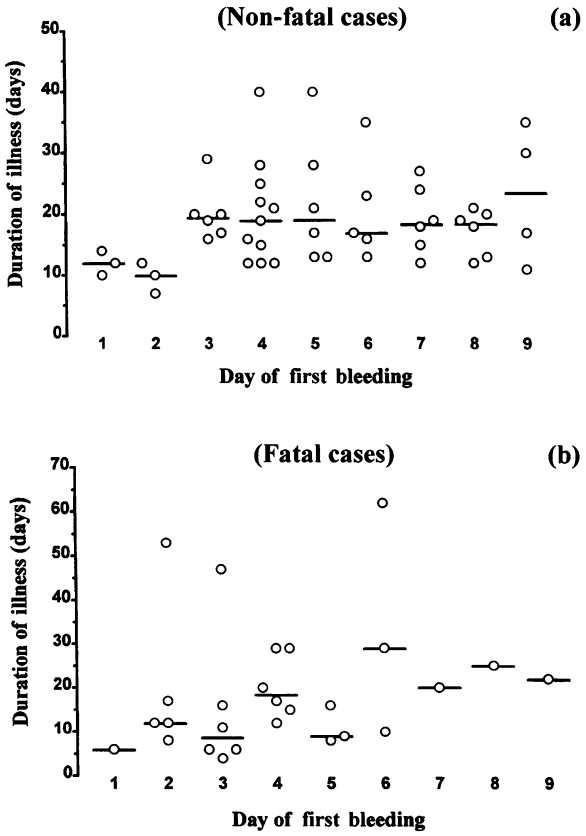

Figure 1 **Effects of bleeding on pleuropneumonia: (*a*) duration of illness in patients who survived, in relation to the day of first bleeding, (*b*) duration of illness in patients who died.**
In both graphs, mean duration of illness in relation to day of first bleeding is indicated by the horizontal line. Data taken from original tables on pp 3 and 10 of Louis' monograph[6].

BLOODLETTING: AN EXAMPLE OF NUMERICAL ANALYSIS

The Louis approach can be best appreciated by looking at the paper in the *American Journal of Medical Sciences*[5]. Louis considered the question as to whether bloodletting was efficacious in reducing the duration of specific disease, pleuropneumonia or pneumonitis. He tabulated his data to indicate the duration of the disease in relation to the day at which the first bleeding was instituted. His argument was simple: if the treatment made any difference at all to the duration of the disease, a measurable outcome, then the earlier it was instituted, the shorter should have been the duration. The comparison groups were patients who had not been bled on that particular day. The data presented in the original tables have been re-fashioned to conform to current practice.

Louis had in total 78 cases of pleuropneumonia in which bloodletting had been instituted. Of these patients, 50 survived and 28 died. He dealt with them separately. Figure 1*a* shows the data gathered on the non-fatal cases. A cursory glance suggests that there are two groups of patients—those in whom bleeding was instituted on the first or second day after diagnosis and those who were bled after the third day. In the former group, the mean duration of illness lay between 10 and 12 days whereas in the latter the mean durations were much longer, ranging from 17 to 23 days. It appeared as though prompt treatment made a difference provided the disease was caught early, but beyond that early phase no benefit accrued.

Louis, however, went to great lengths to caution against this simple-minded interpretation:

> But the amount of difference which exists between these two results, leads us to suspect their exactness; and a thorough examination does in truth show, that the influence of bleeding, when performed within the first two days of the disease, is less than it seems at first sight, and that in general its power is very limited.

He pointed out two deficiencies that appear self-evident to us—the sample size in the early cases and the high degree of variability. He notes that, even when the patients were bled on the same day and where there were sufficient cases (e.g. the fourth day), the duration of illness ranged from 12 to 28.

Benefits of bleeding become even more contentious when one looks at the fatal cases (Figure 1*b*). Of the 28 patients that Louis states he studied (data are shown only for 27), 18 were actually bled within the first four days and only 9 on the next five days. If one considers *all* the cases wherein bleeding was done within the first four days (41 in all), 18 died ('or about three-sevenths') whereas amongst the group that were bled later (36) only 9 died ('or only one-fourth'). This he noted was a startling and absurd result. Using the same data, we can estimate a relative risk of 1.76. Early bleeding could be deadly.

Louis analysed the data critically, commenting not only on the ineffectiveness of bleeding in reducing the duration of the disease but also several other features such as pain, sputum characteristics, crepitation, resonance of voice, and dullness on percussion. He thus concluded that the study of the general and local symptoms, the mortality and variations in the mean duration of the pneumonitis, according to the period at which bloodletting was instituted, 'all establish narrow limits to the utility of this mode of treatment.'

Even from the perspective of this century, Louis' analysis is a striking example of critical thought. His approach and his evangelical zeal in promoting his methods created considerable controversy. It must be remembered that his mentor, Broussais, had been a great proponent of bloodletting and is reported to have used 100 000 leeches a year. Broussais' energetic 'antiphlogistic' doctrines that promoted local bleeding by leeches and a low diet had enormous impact on French medical practice such that France, a leech exporting country in 1820, had exhausted its supplies by 1827 and was importing over 33 million leeches a year, mainly from Hungary and Bohemia (Figure 2)[13].

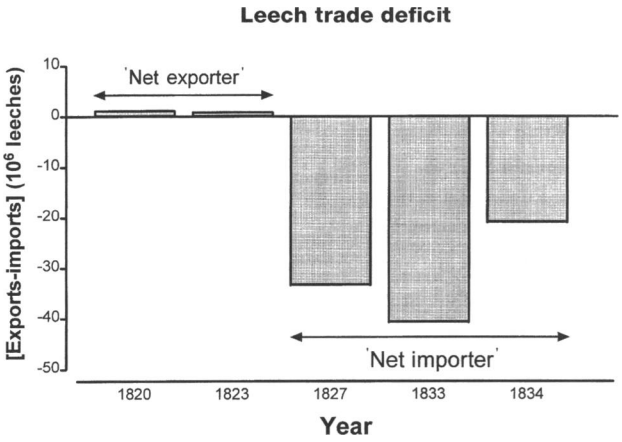

Figure 2 **Changes in leech trade in France between 1800 and 1834.** (Data from Ackerknecht, Reference 13)

THE DOCTRINE SPREADS TO THE NEW WORLD

To Elisha Bartlett and several other American clinicians, the numerical approach appeared as a new light shining in the darkness. Louis attracted foreign disciples, principally American. Oliver Wendell Holmes said they idolized him[13], and Osler[11] noted that these men 'caught his clear accent, learned his great language, made him their model'.

During the 1830s and 1840s, Paris was a medical Mecca for American doctors. More than three hundred seem to have visited Paris during that period. Very few of the visitors were candidates for the French medical degree since most had completed their training before they left for Europe[14,15]. This actually worked to their benefit because Louis was regarded as a poor lecturer and not well suited to beginners in medicine. His hospital, being too far from the medical school, attracted few French students. The American visitors found Louis extremely congenial and they benefited greatly from his experience and teaching methods.

The American disciples of Louis included many from Boston, New York, and Philadelphia and several from the South[10,11,14,15]. The Bostonians figured prominently amongst the proponents of the numerical method and included Wendell Holmes, George C Shattuck Jr, Henry Ingersoll Bowditch and James Jackson Jr. These students with evangelical fervour spread the doctrine of the numerical method. One of the more energetic of Louis' pupils, Henry Bowditch, organized the Boston Society of Medical Observation for discussing cases seen at the Massachusetts General Hospital and in the city[15]. This was similar to one that had been created in Geneva called the Société Médicale d'Observation (with Louis as perpetual president), which functioned as a critical appraisal journal club[10]. Louis' zealous pupils also made their mentor's works available to American readers[15].

NUMERICAL METHOD: CONTROVERSIES ABOUND

The numerical approach, though it appears reasonable from the vantage-point of 1997, was mired in controversy[16]. The arguments against a widespread application of the approach are familiar. The physician called to treat a sick man was not an actuary advising a company to accept or decline 'risks' but someone who dealt with a specific individual at a vulnerable moment[10]. Under such conditions, averages could not help and might even confuse the practising physician as he struggles to apply general rules to a specific case. Practising physicians were unwilling to hold 'their decisions in abeyance till their therapies received numerical approbation.'[17] Further, they were not prepared to discard therapies 'validated by both tradition and their own experience on account of somebody else's numbers.'[17]

The relevance of the numbers themselves was doubted. Although Louis claimed that he merely enumerated, and the entities appeared to be measured objectively, the choice of the particular entities to be measured were subjective, based in some instances only on the clinician's senses[18]. A more serious criticism was that the Louis approach involved mere enumeration, and no effort was made to estimate what would be a significant number of cases or to make allowances for possible error[9,16]. He had not, as Murphy[16] notes, 'devised a test of significance which would indicate success or failure in the competition between rival treatments.' Greenwood[10] wondered what the future of clinical statistics might have been had Louis secured a collaborator such as Poisson. Whether information gathered largely from a hospital population would have any relevance in other contexts seemed uncertain. The Americans appreciated the importance of the epistemological approach but did not believe that the actual knowledge accrued was transferrable. This was particularly so in the realm of therapeutics where American constitutions and diseases were deemed more energetic than those observed in Europe; so, where enfeebled Europeans needed therapeutic elevation, the more robust Americans needed depletion. The doctrine of specificity which held sway argued that variabilities inherent in the disease, the human constitutions and local and regional factors made it difficult to use in American private practice information gathered predominantly from urban poor in large French hospitals[17]. Specific hospitals could attract different cases and one critic noted that paradoxically the number of deaths in a hospital could increase as 'the discipline of the hospital improves, on

account of more severe cases being selected'[19]. The relevance of indulging in the enumeration procedure seemed unclear. Some argued that it would only verify what had been learned from common sense and long experience[19].

Even James Jackson Jr, one of the most ardent disciples of Louis, had some reservations about the general applicability of the procedure and so did his father, a highly respected physician who used the numerical method at Massachusetts General Hospital. In a letter to his son dated 15 January 1832[20], the senior physician noted that, though statistics were valuable, the 'man who places great reliance on them in any branch of science, physical, moral, or political, is apt to make the mistake of thinking that two and two always make four—which they do not. That is he applies mathematical reasoning to subjects which do not admit it'.

Louis defended his position on several of these issues, particularly against the charge that by grouping cases he ignored the uniqueness of each patient. He argued that it depended upon the extent of the similarity one is looking for. 'A leaf of a tree once well described may always be recognised' and thus one 'can form a class of facts bearing sufficient resemblance, one to another, and from hence deduce laws which every day's experience verifies'. He also noted that experience showed that 'a truly efficacious medicine will exercise its influence in spite of differences in those to whom it is administered; the disease itself seeming to efface such differences.'[6]

Large numbers and enumeration were necessary to equalize differences since 'by so doing, the errors (which are inevitable), being the same in two groups of patients subjected to different treatment, mutually compensate each other, and they may be disregarded without sensibly affecting the exactness of the results'.

The charge that one cannot precisely fix the onset or termination of the disease was one that Louis took seriously, though he argued that symptoms/signs can be used to assess the onset. He also noted that it may be just as difficult to fix the termination of the disease, but this too must be done.

The approach Louis used was a simple one. He was by no means the first. In his empirical approach and distrust of hypotheses he followed a lineage that included Hippocrates, the Alexandrian Empiricists, Paracelsus and Sydenham[9,21]. His enumerative approach was not entirely novel either. Pinel had adopted a similar approach when he demonstrated the value of 'moral treatment' and, during the 1820s and 1830s, many physicians concerned with issues of public health and hygiene were looking at numbers that testified to the presence of diverse contributing factors. What distinguished Louis from other empiricists was that there was a programme, and though the French were empiricists they were not 'mere empirics'[22]. They believed that diseases were objective realities and factors could be discerned. In addition, Louis was good at being a propagandist and ensuring that his views were heard through his students, particularly the ones from abroad.

EVIDENCE-BASED MEDICINE: WHAT EVIDENCE AND WHOSE?

The arguments made here suggest that, in several ways, the proponents of the numerical method were advocating an evidence-based medicine of their own kind. In their insistence on measured outcomes, the reference to accumulated facts and an essentially empirical approach, they bear a resemblance to the ardent proponents of evidence-based medicine of today. In response to the hyperbole and evangelical zeal of the American disciples of Louis, an irate physician wrote in the pages of the *Boston Medical and Surgical Journal* that the claim that disease had been investigated for the first time by the French stars was equivalent to saying that eminent physicians of the past 'knew nothing about induction or generalisation, were ignoramuses in pathology and therapeutics, unable to reason correctly, and that their works are less than useless to the medical student'[17].

Today, the designation of one system of medicine as evidence-based implies that other systems are not based on evidence. This is far from true. What is at stake is not the presence or absence of evidence but the legitimacy of the evidence used to justify clinical decisions. Bates[23] contrasts the relationship between the knower and the known in several different medical systems. He notes that in the traditional systems (e.g. Chinese or Ayurvedic systems) greater emphasis is placed on the knower, and knowledge is legitimized by his status based on his learning and experience. In contrast, other systems are centred on what is known. How the information was acquired is important. Bates used the terms gnostic and epistemic to distinguish between the systems that emphasize the knower and the known, respectively. Clearly such a sharp contrast is more theoretical than realistic. Even in contemporary medicine—an example of epistemic knowing *par excellence*—training and track record do add to credibility. Ironically, even the McMaster Group who are evangelical about evidence-based medicine advise readers of publications to consider the author's track record[24]. If the material is really sound, does it matter who says it?

In a reflective editorial, Carr-Hill[4] discusses wryly the problems in dealing with the tenets of evidence-based medicine:

'No one denies the importance of evidence: it is a *sine qua non* of professional practice. But often, there are no simple answers to apparently simple questions: there is a role for judgement in decision-making—just as in criminal law trials both prosecution and

defence try to build a convincing picture to place before the jury. But this does not mean that lawyers or juries ignore the evidence: indeed, would it not have been seen as rather silly to promote "evidence-based law"?'

REFERENCES

1 Davidoff F, Haynes B, Sackett D, Smith R. Evidence based medicine. *BMJ* 1995;**310**:1085–6

2 Carr-Hill R. Welcome? To the brave new world of evidence based medicine. *Soc Sci Med* 1995;**41**:1467–8

3 Rosenberg W, Donald A. Evidence based medicine: an approach to clinical problem-solving. *BMJ* 1995;**310**:1122–6

4 Grahame-Smith D. Evidence based medicine: Socratic dissent. *BMJ* 1995;**310**:1126–7

5 Louis PCA. Researches on the effects of blood-letting in some inflammatory diseases, and on the influence of tartarised antimony and vesication in pneumonitis. *Am J Med Sci* 1836;**18**:102–11

6 Louic PCA. *Researches on the Effects of Bloodletting in Some Inflammatory Diseases and on the Influence of Tartarised Antimony and Vesication in Pneumonitis*, Translated by CG Putnam. Boston: Hilliard, Gray, 1836

7 Bollet AJ. Pierre Louis: the numerical method and the foundation of quantitative medicine. *Am J Med Sci* 1973;**266**:93–101

8 Steiner WR. Dr. Pierre-Charles-Alexander Louis, a distinguished Parisian teacher of American medical students. *Ann Med History* 1940;**II**:451–60

9 Rosen G. P.C.A. Louis. *Int Encylopedia Soc Sci* 1968;**9**:478–9

10 Greenwood M. Louis and the numerical method. In: *The Medical Dictator and other Biographical Studies*. London: Williams & Northgate, 1936:123–41

11 Osler W. The Influence of Louis on American Medicine. In: *An Alabama Student and Other Biographical Essays*. New York: Oxford University Press, 1909:189–210

12 Louis PCA. Medical statistics. *Am J Med Sci* 1837;**21**:525–8

13 Ackerknecht EH. *Medicine at the Paris Hospital 1794–1848*. Baltimore: Johns Hopkins Press, 1967:62

14 Jones RM. American doctors in Paris, 1820–1861: a statistical profile. *J Hist Med* 1970;April:143–57

15 Jones RM. American doctors and the Parisian medical world, 1830–1840. *Bull Hist Med* 1973;**47**:177–204

16 Murphy TD. Medical knowledge and statistical methods in early nineteenth-century France. *Med History* 1981;**25**:310–19

17 Warner JH. Attitudes to Foreign Knowledge. In: *The Therapeutic Perspective: Medical Practice, Knowledge, and Identity in America*, 1820–1835. Cambridge, MA: Harvard University Press, 1986:185–206

18 Shryock RH. The history of quantification in medical science. *Isis* 1961;**52**:215–37

19 Goldberg JP. The numerical method: how it struck a contemporary. *Isis* 1963;**54**:133–5

20 Putnam JJ. *A Memoir of Dr. James Jackson*. London: Cambridge University Press, 1905:332

21 Ackernecht EH. Recurrent themes in medical thought. *Sci Monthly* 1949;**69**:80–3

22 Shryock RH. Medicine and society in transition 1820–1860. In: *Medicine and Society in America: 1660–1860*. New York: New York University Press, 1960:126

23 Bates D. *Scholarly Ways of Knowing: An Introduction in Knowledge and the Scholarly Medical Traditions*. Cambridge: Cambridge University Press, 1995:1–22

24 Department of Clinical Epidemiology and Biostatistics, McMaster University Health Sciences Centre. How to read clinical journals: I. Why to read them and how to start reading them critically. *Can Med Assoc J* 1981;**124**:555–8